TRANSMITTAL LETTER

Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

Metastasis

Application of:

Karl Tryggvason

10/695,559

Title: Use of Antibodies to the Gamma 2 Chain of Laminin 5 to Inhibit Tumor Growth and

Dear Sir:

Serial No.

Filed:

In regard to the above-identified U.S. patent application;

- 1. We are transmitting herewith the attached:
 - a) Transmittal Letter
 - b) Information Disclosure Statement (IDS) (11 sheets);
 - IDS Form 1449 (5 sheets); c)
 - Copy of International Search Report of PCT/EP03/12012 (7 sheets); d)
 - 87 cited References e)
 - f) Return Receipt Postcard.
- 2. With respect to fees:
 - a) No fee is required.
 - b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.
- 3. CERTIFICATE OF MAILING BY "EXPRESS MAIL" UNDER 37 CFR § 1.10: The undersigned hereby certifies that this Transmittal Letter and the papers, as described hereinabove, are being deposited with the United States Postal Service with sufficient postage as "Express Mail Post Office to Addressee" in a box addressed to: PO Box 1450, Alexandria, VA 22313-1450, on this 30th day of June , 2004. Express Mail No. EV334706135US.

Respectfully submitted,

Registration No. 42,636





IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (Case No. 02-1147-US)

In the Application of: Tyggvason et al.)
) Art Unit: To be assigned
)
Serial No. 10/695,559) Examiner: To be assigned
)
Filed: October 28, 2003)
)
Title: Use of Antibodies to the Gamma 2 Chain of)
Laminin 5 to Inhibit Tumor Growth and)
Metastasis	j

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references of record in the above-identified application. This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. Copies of the references cited below are enclosed. In the judgment of the undersigned, portions of the listed references may be material to the Examiner's consideration of the presently pending claims. However, the references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative relevance between references, whether cited in this or prior statements. This statement is not a representation that the listed references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. Section 102 or Section 103.

	This information Disclosure Statement is being filed:
	within three months of the filing date of a national application; within three months of the date of entry into the national stage as set forth in 37 C.F.R. § 1.491 in an international application; or before the mailing date of a first Office Action on the merits. 37 C.F.R. §1.97 (b)
	after three months of the filing date of a national application, or the date of entry into the national stage as set forth in 37 C.F.R. § 1.491 in an international application; or after the mailing date of a first Office Action on the merits, but <u>before</u> the mailing date of a Final Action under 37 C.F.R. § 1.113 or a Notice of Allowance under 37 C.F.R. § 1.311 (whichever occurs first), and includes (37 C.F.R. § 1.97 (c):
	the Certification under 37 C.F.R. § 1.97(e) (see "Certification" below)
	OR
	the fee of \$180 set forth in 37 C.F.R. § 1.17(p) (see "Fees" below).
	after a Final Action under 37 C.F.R. § 1.113 or a Notice of Allowance under 37 C.F.R. § 1.311 (whichever occurs first), but before, or simultaneously with, the payment of the issue fee, and includes the Certification under 37 C.F.R. § 1.97(e) (see "Certification" below), and the Petition Fee set forth in 37 C.F.R. § 1.17(i) (see "Fees" and "Method of Payment of Fees" below). Applicants hereby petitions for consideration of the Information Disclosure Statement submitted herewith and the accompanying references in examination of the subject patent application.
CERT	<u>IFICATION</u>
	The undersigned hereby certifies that each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.
	The undersigned hereby certifies that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application or, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of the Information Disclosure Statement

U.S. Serial No.: <u>10/695,559</u> Filing Date: <u>October 28, 2003</u>

<u>FEES</u>	No fee is owed by the applicant(s). The IDS Fee of \$180.00 under 37 C.F.R. §	1.17(p) is enclosed herewith.
METH	Attached is a check in the amount of \$180.0 Charge Deposit Account No. 13-2490 in the communication is enclosed for that purpose.	amount of \$. (A duplicate copy of this
comm		ny overpayment in connection with this A duplicate copy of this communication is
this co with th an env 1450,	rrespondence and all attached paper(s) or fee ne United States Postal Service as EXPRESS relope addressed to: Commissioner for Pate	MAIL" (37 CFR 1.10) I hereby certify that $e(s)$ is being deposited with sufficient postage, MAIL POST OFFICE TO ADDRESSEE in ints, P.O. Box 1450, Alexandria, VA 22313-
Date:	6/30/04	David S. Harper Registration No. 42,636
•	none: 312-913-0001 nile: 312-913-0002	McDonnell Boehnen Hulbert & Berghoff 300 South Wacker Drive Chicago,IL 60606

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I. United States Patents

- 1. Strom, T.B. et al., U.S. Patent No. 5,152,980, Issued: Oct. 6, 1992.
- 2. Tryggvason, et al., U.S. Patent No. 5,660,982, Issued: Aug. 26, 1997.
- 3. Jones, et al., U.S. Patent No. 6,294,356, Issued: Sept. 25, 2001.
- 4. Tryggvason, et al., U.S. Patent No. 6,143,505, Issued: November 7, 2000.
- 5. Tryggvason, et al., U.S. Published Application No. 2002/0052307, Published on May 2, 2002.

II. Foreign Patent

6.	WO 00/26342	Published:	May 11, 2000
7.	WO 00/34441	Published:	June 15, 2000
8.	WO 01/87239	Published:	Nov. 22, 2001
9.	WO 02/30465	Published:	April 18, 2002
10	. WO 03/016907	Published:	February 27, 2003

III. Other documents

- 11. Aberdam, D. et al., (1994), Nature Genetics, "Herlitz's junctional epidermolysis bullosa is linked to mutations in the gene (LAMC2) for the y2 subunit of nicein/kalinin (Laminin-5)" 6(3):299-304
- 12. Buto, S. et al., (1998), EMBASE No. 97163048, "Production and characterization of monoclonal antibodies directed against the laminin receptor precursor."
- 13. Giannelli, G. et al., (1997), Science, "Induction of cell migration by matrix metalloprotease-2 cleavage of laminin-5" 277:225-228.
- 14. Hao, et al., (1996), Am. J. Pathol. "Differential Expression of laminin 5 ($\alpha 3\beta 3\gamma 2$) by human malignant and normal prostate" 149:1341-49.
- 15. Hellman, K., et al., (2000), Int J. Gynecol Cancer, "Cancer of the Vagina: Laminin- 5γ 2 Chain Expression and Prognosis", Vol. 10, pp. 391-396.
- 16. Kallunki, et al., (1992), J. Cell Biol. "A truncated laminin chain homologous to the β2 chain: structure, spatial expression, and chromosomal assignment" 119: 679-93.
- 17. Larjava, et al., (1993), J. Clin. Invest. "Expression of integrins and basement membrane components by wound keratinocytes" 92:1425-35.
- 18. Martin, et al., (1998), Mol. Med. "Down-regulation of laminin-5 in breast carcinoma cells" 4:602-13.

McDonnell, Boehnen, Hulbert & Berghoff LLP 300 S. Wacker Drive, Suite 3100 Chicago, IL 60606 312-913-0001

- 19. Matsui, C. et al., (1995), J. Investigative Dermatology, "γ2 chain of laminin-5 is recognized by monoclonal antibody GB3" 105(5):648-652.
- 20. Nissinen, M. et al., (1991), Biochem. J. "Primary structure of the human laminin A chain" 276:369-379.
- 21. Orian-Rousseau, et al., (1993), J. Cell. Sci. "Human colonic cancer cells synthesize and adhere to laminin-5. Their adhesion to laminin-5 involves multiple receptors among which is integrin α2β1" 111:1993-2004.
- 22. Pelletier, et al., (1996), J. Biol. Chem. "Activation of the integrin αvβ3 involves a discrete cation-binding site that regulates conformation" 271:1364.
- 23. Pikkarainen, T. et al., (1987), J. Biol. Chem. "Human laminin B1 chain" 262:10454-10462.
- 24. Pikkarainen, T. et al., (1988), J. Biol. Chem. "Human laminin β2 chain" 263:6751-6758.
- 25. Pulkkinen, L. et al. (1994), Nature Genetics, "Mutations in the γ 2 chain gene (LAMC2) of kalinin/laminin 5 in the junctional forms of epidermolysis bullosa" 6(3):293-298.
- 26. Pyke, et al., (1994), Am. J. Pathol. "Laminin-5 is a marker of invading cancer cells in some human carcinomas and is coexpressed with the receptor for urokinase plasminogen activator in budding cancer cells in colon adenocarcinomas" 145:782-91.
- 27. Pyke, et al., (1995), Cancer Res. "The γ 2 chain of kalinin/laminin 5 is preferentially expressed in invading malignant cells in human cancers" 55:4132-39.
- 28. Seaver, S. S. (1994), Genetic Engineering News, "Monoclonal antibodies in industry: more difficult than originally thought" August 10 issue, pp20-21.
- 29. Sordat, et al., (1998), J. Pathol. "Differential expression of laminin-5 subunits and integrin receptors in human colorectal neoplasia" 185:44-52.
- 30. Tani, et al., (1996), Am. J. Pathol. "α6β4 integrin and newly deposited laminin-1 and laminin-5 form the adhesion mechanism of gastric carcinoma" 149:781-93.
- 31. Tryggvason, K. (1993), Current Opinion in Biol. "The laminin family" 5:877-882.
- 32. Vailly, J. et al. (1994), Eur. J. Biochem. "The 100-kDa chain of nicein/kalinin is a laminin β2 chain variant" 219:209-218.

- 33. Verrando, P. et al., (1991), Lab. Invest. "Monoclonal antibody GB3 defines a widespread defect of several basement membranes and a keratinocyte dysfunction in patients with lethal junctional epidermolysis bullosa" 64:85-92.
- 34. Verrando, P. et al., (1993), J. Investigative Dermatology, "Nicein (BM-600) in junctional epidermolysis bullosa: polyclonal antibodies provide new clues for pathogenic role" 101(5):738-743.
- 35. Vuolteenaho, R. (1994), J. Cell Biol. "Human laminin M chain (merosin): complete primary structure, chromosomal assignment, and expression of the M and A chain in human fetal tissues" 124:381-394.
- 36. Wewer, U. M. et al., (1992), Lab. Invest. "Laminin A, B1, B2, S and M subunits in the postnatal rat liver development and after partial hepatectomy" 66:378-389.
- 37. Amano, et al., (2000), The Journal of Biological Chemistry, "Bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ 2 chain", Vol. 275(30), pp. 22728-22735.
- 38. Anderson, et al., (2001), The Laryngoscope, "Tumor deposition of laminin-5 and the relationship with perineural invasion", Vol. 111, pp. 2140-2143.
- 39. Calaluce, et al., (2001), Molecular Carcinogenesis, "Laminin-5-mediated gene expression in human prostate carcinoma cells", Vol. 30, pp. 119-129.
- 40. Davis, et al., (2001), The Prostate, "Unique expression pattern of the $\alpha6\beta4$ integrin and Laminin-5 in human prostate carcinoma", Vol. 46, pp. 240-248.
- 41. Engvall, et al., (1990), Cell Regulation, "Distribution and isolateion of four laminin variants; tissue restricted distribution of heterotrimers assembled from five different subunits", Vol. 1, pp. 731-740.
- 42. Fukushima, et al., (2001), Mod. Pathol., "Expression of laminin-5- γ -2 chain in intraductal papillary-mucinous and invasive ductal tumors of the pancreas", Vol. 14(5), pp. 404-409.
- 43. Gianelli and Antonaci, (2001), Clinical and Experimental Metastasis, "Biological and Clinical Relevance of Laminin-5 in Cancer", Vol. 18, pp. 439-443.
- 44. Goldfinger, et al., (1998), J. Cell Biol., "Processing of Laminin-5 and its functional consequences: Role of Plasmin and Tissue-type Plasminogen Activator", Vol. 141, pp. 255-265.
- 45. Gonzales, et al., (1999), Mol. Biol. of the Cell, "A cell signal pathway involving laminin-5, $\alpha 3\beta 1$ integrin, and mitogen-activated protein kinase can regulate epithelial cell proliferation", Vol: 10, pp. 259-270.

- 46. Grassi, et al., (1999), Journal of Cell Science, "The SFL activity secreted by metastatic carcinoma cells is related to laminin 5 and mediates cell scattering in an integrinindependent manner", Vol. 112, pp. 2511-2520.
- 47. Haas, et al., (2001), The Journal of Histochemistry & Cytochemistry, "A comparative quantitative analysis of laminin-5 in the basement membrane of normal, hyperplastic, and malignant oral mucosa by confocal immunofluorescence imaging", Vol. 49(10), pp. 1261-1268.
- 48. Habermann, et al., (2001), Scand J. Gastroenterol, "Ulcerative colitis and colorectal carcinoma", Vol. 7, pp. 751-758.
- 49. Heagerty, et al., (1986), Lancet, "GB3 monoclonal antibody for diagnosis of junctional epidermolysis bullosa", Vol. 860, page 8485.
- 50. Heagerty, et al., (1987), British J. Dermatol, "Raid prenatal diagnosis of epidermolysis bullosa letalis using GB3 monoclonal antibody", Vol. 17, pp. 271-275.
- 51. Henning, et al., (1999), Histopathology, "Loss of laminin-5 in the epithelium-stroma interface: an immunohistochemical marker of malignancy in epithelial lesions of the breast", Vol: 34, pp. 305-309.
- 52. Hlubek, et al., (2001), Cancer Research, "Expression of the invasion factor laminin γ 2 in colorectal carcinomas is regulated by β -catenin¹", Vol. 61, pp. 8089-8093.
- 53. Hsi, et al., (1986), J. Reprod. Immunology, "Monoclonal antibodies to human amnion", Vol: 9, pp. 11-21.
- 54. Kagesato, et al., (2001), Japan J. Cancer Research, "Sole expression of laminin γ 2 chain in invading tumor cells and its associateion with stromal fibrosis in lung adenocarcinomas", Vol. 21, pp. 184-192.
- 55. Katoh, et al., (2002), Oncology, "Correlation between laminin-5 γ 2 chain expression and epidermal growth factor receptor expression and its clinicopathological significance in squamous cell carcinoma of the tongue, Vol: 62, pp. 318-326.
- 56. Koshikawa, et al., (1999), Cancer Research, "Overexpression of laminin γ 2 chain monomer in invading gastric carcinoma cells, Vol: 59, pp. 5596-5601.
- 57. Lenander, et al., (2001), Analytical Cellular Pathology, "Laminin-5 γ 2 chain expression correlates with unfavorable prognosis in colon carcinomas", Vol. 22, pp. 201-209.

- 58. Lohi, et al., (2000), APMIS, "Basement membrane laminin-5 is deposited in colorectal adenomas and carcinomas and serves as a ligand for $\alpha \beta 1$ integrin", Vol. 108, pp. 161-172.
- 59. Lugassy, et al., (1999), J. Cutaneuous Pathol., "Tumor microvessels in melanoma express the beta-2 chain of laminin. Implications for melanoma metastasis", Vol. 26, pp. 222-226.
- 60. Määttä, et al., (2001), The Journal of Histochemistry & Cytochemistry, "Comparative analysis of the distribution of laminin chains in the basement membranes in some malignant epithelial tumors: The αl chain of laminin shows a selected expression pattern in human carcinomas", Vol: 49(6), pp. 711-725.
- 61. Määttä, et al., (1999), Journal of Pathology, "Expression of the laminin γ 2 chain in different histological types of lung carcinoma. A study by immunohistochemistry and *in situ* hybridization", Vol: 188, pp. 361-368.
- 62. Manda, et al., (2000), Biochemical and Biophysical Research Communications, "Differential expression of the LAMB3 and LAMC2 genes between small cell and non-small cell lung carcinomas", Vol. 275, pp. 440-445.
- 63. Marinkovich, et al., (1992), JBC, "The anchoring filament protein kalinin is synthesized and secreted as a high molecular weight precursor", Vol. 267, pp. 17900-17906.
- 64. McMillan, et al., (1997), Br. J. Dermatol., "Immunohistochemical analysis of the skin in junctional epidermolysis bullosa using laminin 5 chain specific antibodies is of limited value in predicting the underlying gene mutation", Vol: 136, pp. 817-822.
- 65. Mizushima, et al., (1998), Horm. Res., "Wide Distribution of Laminin-5 γ chain in basement membranes of various human tissues", Vol. 50 (Suppl. 2), pp. 7-14.
- 66. Mizushima, et al., (1996), J. Biochem., "Differential expression of laminin-5/ladsin subunits in human tissues and cancer cell lines and their induction by tumor promoter and growth factors", Vol. 120, pp. 1196-1202.
- 67. Moriya, et al., (2001), Cancer, "Increased expression of laminin-5 and its prognostic significance in lung adenocarcinomas of small size", Vol. 19(6), pp. 1129-1141.
- 68. Niki, et al., (2002), American Journal of Pathology, "Frequent co-localization of cox-2 and laminin-5 γ 2 chain at the invasive front of early-stage lung adenocarcinomas", Vol: 160(3), pp. 1129-1130.
- 69. Nordemar, et al., (2001), Anticancer Research, "Laminin-5 as a predictor of invasiveness in cancer *in situ* lesions of the larynx", Vol. 21, pp. 509-512.

U.S. Serial No.: 10/695,559

Filing Date: October 28, 2003

- 70. Nordstrom, et al., (2002), Int. J. Gynecol., "Laminin-5 γ 2 chain as an invasivity marker for uni-and multifocal lesions in the lower anogenital tract", Vol. 12, pp. 105-109.
- 71. Ono, et al., (2002), Cancer Letters, "Epidermal growth fctor receptor gene amplification is correlated with laminin-5 γ 2 chain expression in oral squamous cell carcinoma cell lines", Vol: 175, pp. 197-204.
- 72. Patarroyo, et al., (2002), Cancer Biology, "Laminin isoforms in tumor invasion, angiogenesis and metastasis", Vol. 12, pp. 197-207.
- 73. Patel, et al., (2002), Int. J. Cancer, "Laminin- γ 2 overexpression in head-and-neck squamous cell carcinoma", Vol. 99, pp. 583-588.
- 74. Rouselle, et al., (1991), J. Cell Biol., "Kalinin: an epithelium-specific basement membrane adhesion molecule that is a component of anchoring filaments", Vol. 114(3), pp. 567-576.
- 75. Rouselle, et al., (1994), J. Cell Biol., "Kalinin is more efficient than laminin in promoting adhesion of primary keratinocytes and some other epithelial cells and has a different requirement of integrin receptors", Vol. 125, pp. 205-214.
- 76. Salo, et al., (1999), Matrix Biol., "Laminin-5 promotes adhesion and migration of epithelial cells: identification of a migration-related element in the γ 2 chain gene (LAMC2) with activity in transgenic mice", Vol. 18, pp. 197-210.
- 77. Salo, et al., (1999), Acta Univ. Oul.D 540, "Laminin-5: Function of the γ 2 chain in epithelial cell adhesion and migration, and expression in epithelial cells and carcinomas" Doctoral Dissertation.
- 78. Seftor, et al., (2001), Cancer Research, "Cooperative interactions of laminin 5 γ 2 chain, matrix metalloproteinase-2, and membrane type-1-matrix/metalloproteinase are required for mimicry of embryonic vasculogenesis by aggressive melanoma", Vol. 61, pp. 6322-6327.
- 79. Skyldberg, et al., (1999), Journal of the National Cancer Institute, "Laminin-5 as a marker of invasiveness in cervical lesions", Vol. 91(21), pp. 1882-1887.
- 80. Soini, et al., (1996), Journal of Pathology, "Expression of the laminin γ 2 chain in pancreatic adenocarcinoma", Vol. 180, pp. 290-294.
- 81. Sordat, et al., (2000), Int. J. Cancer., "Tumor cell budding and Laminin-5 expression in colorectal carcinoma can be modulated by the tissue micro-environment", Vol. 88, pp. 708-717.

9

U.S. Serial No.: <u>10/695,559</u> Filing Date: <u>October 28, 2003</u>

- 82. Takahashi, et al., (2002), Cancer, Cytoplasmic Expression of Laminin γ 2 Chain Correlates with Postoperative Hepatic Metastasis and Poor Prognosis in Patients with Pancreatic Ductal Adenocarcinoma", Vol: 94(6), pp. 1894-1901.
- 83. Tani, et al., (1997), American Journal of Pathology, "Pancreatic carcinomas deposit laminin-5 preferably adhere to laminin-5, and migrate on the newly deposited basement membrane", Vol: 151(5), pp. 1289-1302.
- 84. Tsuji, et al., (2002), Clinical & Experimental Metastasis, "Regulation of melanoma cell migration and invasion by laminin-5 and $\alpha 3\beta 1$ integrin (VLA-3), Vol: 19, pp. 127-134.
- 85. Tunggal, et al., (2002), American Journal of Pathology, "Defective laminin 5 processing in cylindroma cells", Vol: 160(2), pp. 459-468.
- 86. Verrando, et al., (1987), Exp. Cell Res., "Monoclonal antibody GB3, a new probe for the study of human basement membranes and hemidesmosomes", Vol: 170, page 116-128.
- 87. Yamamoto, et al., (2001), Clinical Cancer Research, "Expression of the γ 2 chain of Laminin-5 at the invasive front is associated with recurrence and poor prognosis in human esophageal squamous cell carcinoma", Vol. 7, pp. 896-900.

IV. The Applicants hereby notify The Patent Office of the following co-pending applications:

	Serial No.	Filing <u>Date</u>	<u>Author</u>	Attorney <u>Docket No.</u>
1.	09/756,071	Jan. 8, 2001	Tryggvason et al.	02-1239-A

V. <u>Discussion</u>

In accordance with MPEP Sections 609 and 707.05(b), it is requested the documents cited be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with.

U.S. Serial No.: 10/695,559

Filing Date: October 28, 2003

This is requested so that each document becomes listed on the face of the patent issuing on the present application.

Date: June 30, 2004

By:

David Harper Reg. No. 42,636

McDonnell, Boehnen **Hulbert & Berghoff** 300 South Wacker Drive Chicago, IL 60606

U.S. Serial No.: 10/695,559

Filing Date: October 28, 2003

Respectfully Submitted,

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FORM	PTO-1449
(Rev. 2	2-32)

U.S. Department of Commerce Patent and Trademark Office

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INFORMATION DISCL	OSURE
STATEMENT BY APP	LICANT
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Atty. Docket No.	Serial No.
02-1147-US	10/695,559

Applicant: Tyggvason et al.

Filing Date: October 28, 2003 **Group:** To be Assigned

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1.	5,152,980	10/6/92	Strom, T. B. et al.			5/18/89
	2.	5,660,982	8/26/97	Tryggvason, et al.			10/4/94
	3.	6,294,356	9/25/01	Jones, et al.			1/15/99
	4.	6,143,505	11/7/00	Tryggvason, et al.			2/18/97
	5.	2002/0052307	2/27/03	Tryggvason, et al.			1/8/01

FOREIGN PATENT DOCUMENTS

						Trans	slation
	Document Number	Date	Country	Class	Subclass	Yes	No
6.	WO 00/26342	5/11/00	PCT			X	
 7.	WO 00/34441	6/15/00	PCT			Х	
8.	WO 01/87239	11/22/01	PCT			Х	
9.	WO 02/30465	4/18/02	PCT			Х	
10.	WO 03/016907	2/27/03	PCT				Х

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

	11.	Aberdam, D. et al., (1994), Nature Genetics, "Herlitz's junctional epidermolysis bullosa is linked to mutations in the gene (LAMC2) for the γ2 subunit of nicein/kalinin (Laminin-5)" 6(3):299-304
	12.	Buto, S. et al., (1998), EMBASE No. 97163048, "Production and characterization of monoclonal antibodies directed against the laminin receptor precursor."
:	13.	Giannelli, G. et al., (1997), Science, "Induction of cell migration by matrix metalloprotease-2 cleavage of laminin-5" 277:225-228.
	14.	Hao, et al., (1996), Am. J. Pathol. "Differential Expression of laminin 5 (α3β3γ2) by human malignant and normal prostate" 149:1341-49.
	15.	Hellman, K., et al., (2000), Int. J. Gynecol cancer, "Cancer of the Vagina: Laminin-5γ2 Chain Expression and Prognosis", Vol. 10, pp. 391-396.

EXAMINER	DATE CONSIDERED

	16.	Kallunki, et al., (1992), J. Cell Biol. "A truncated laminin chain homologous to the β2 chain: structure, spatial expression, and chromosomal assignment" 119: 679-93.
	17.	Larjava, et al., (1993), J. Clin. Invest. "Expression of integrins and basement membrane components by wound keratinocytes" 92:1425-35.
	18.	Martin, et al., (1998), Mol. Med. "Down-regulation of laminin-5 in breast carcinoma cells" 4:602-13.
	19.	Matsui, C. et al., (1995), J. Investigative Dermatology, "γ2 chain of laminin-5 is recognized by monoclonal antibody GB3" 105(5):648-652.
	20.	Nissinen, M. et al., (1991), Biochem. J. "Primary structure of the human laminin A chain" 276:369-379.
	21.	Orian-Rousseau, et al., (1993), J. Cell. Sci. "Human colonic cancer cells synthesize and adhere to laminin-5. Their adhesion to laminin-5 involves multiple receptors among which is intergrin α2β1" 111:1993-2004.
	22.	Pelletier, et al., (1996), J. Biol. Chem. "Activation of the integrin ανβ3 involves a discrete cation-binding site that regulates conformation" 271:1364.
	23.	Pikkarainen, T. et al., (1987), J. Biol. Chem. "Human laminin B1 chain" 262:10454-10462.
	24.	Pikkarainen, T. et al., (1988), J. Biol. Chem. "Human laminin β2 chain" 263:6751-6758.
•	25.	Pulkkinen, L. et al. (1994), Nature Genetics, "Mutations in the γ2 chain gene (LAMC2) of kalinin/laminin 5 in the junctional forms of epidermolysis bullosa" 6(3):293-298.
	26.	Pyke, et al., (1994), Am. J. Pathol. "Laminin-5 is a marker of invading cancer cells in some human carcinomas and is coexpressed with the receptor for urokinase plasminogen activator in budding cancer cells in colon adenocarcinomas" 145:782-91.
	27.	Pyke, et al., (1995), Cancer Res. "The γ2 chain of kalinin/laminin 5 is preferentially expressed in invading malignant cells in human cancers" 55:4132-39.
	28.	Seaver, S. S. (1994), Genetic Engineering News, "Monoclonal antibodies in industry: more difficult than originally thought" August 10 issue, pp20-21.
	29.	Sordat, et al., (1998), J. Pathol. "Differential expression of laminin-5 subunits and integrin receptors in human colorectal neoplasia" 185:44-52.
	30.	Tani, et al., (1996), Am. J. Pathol. "α6β4 integrin and newly deposited laminin-1 and laminin-5 form the adhesion mechanism of gastric carcinoma" 149:781-93.
	31.	Tryggvason, K. (1993), Current Opinion in Biol. "The laminin family" 5:877-882.
	32.	Vailly, J. et al. (1994), Eur. J. Biochem. "The 100-kDa chain of nicein/kalinin is a laminin β2 chain variant" 219:209-218.
	33.	Verrando, P. et al., (1991), Lab. Invest. "Monoclonal antibody GB3 defines a widespread defect of several basement membranes and a keratinocyte dysfunction in patients with lethal junctional epidermolysis bullosa" 64:85-92.
	34.	Verrando, P. et al., (1993), J. Investigative Dermatology, "Nicein (BM-600) in junctional epidermolysis bullosa: polyclonal antibodies provide new clues for pathogenic role" 101(5):738-743.

EXAMINER	DATE CONSIDERED

35	Vuolteenaho, R. (1994), J. Cell Biol. "Human laminin M chain (merosin): complete primary structure chromosomal assignment, and expression of the M and A chain in human fetal tissues" 124:381-394.
36	Wewer, U. M. et al., (1992), Lab. Invest. "Laminin A, B1, B2, S and M subunits in the postnatal rat live development and after partial hepatectomy" 66:378-389.
37	Amano, et al., (2000), The Journal of Biological Chemistry, "Bone morphogenetic protein 1 is an extracellular processing enzyme of the laminin 5 γ 2 chain", Vol. 275(30), pp. 22728-22735.
38	Anderson, et al., (2001), The Laryngoscope, "Tumor deposition of laminin-5 and the relationship with perineura invasion", Vol: 111, pp. 2140-2143.
39	Calaluce, et al., (2001), Molecular Carcinogenesis, "Laminin-5-mediated gene expression in human prostate carcinom cells", Vol. 30, pp. 119-129.
40	carcinoma", Vol. 46, pp. 240-248.
41	Engvall, et al., (1990), Cell Regulation, "Distribution and isolateion of four laminin variants; tissue restricted distribution of heterotrimers assembled from five different subunits", Vol. 1, pp. 731-740.
42	Fukushima, et al., (2001), Mod. Pathol., "Expression of laminin-5-γ-2 chain in intraductal papillary-mucinous an invasive ductal tumors of the pancreas", Vol. 14(5), pp. 404-409.
43	Gianelli and Antonaci, (2001), Clinical and Experimental Metastasis, "Biological and Clinical Relevance of Laminin-5 i Cancer", Vol. 18, pp. 439-443.
44	Goldfinger, et al., (1998), J. Cell Biol., "Processing of Laminin-5 and its functional consequences: Role of Plasmin and Tissue-type Plasminogen Activator", Vol. 141, pp. 255-265.
45	Gonzales, et al., (1999), Mol. Biol. of the Cell, "A cell signal pathway involving laminin-5, $\alpha \beta \beta$ 1 integrin, and mitogen activated protein kinase can regulate epithelial cell proliferation", Vol. 10, pp. 259-270.
46	Grassi, et al., (1999), Journal of Cell Science, "The SFL activity secreted by metastatic carcinoma cells is related to laminin 5 and mediates cell scattering in an integrin-independent manner", Vol. 112, pp. 2511-2520.
47	Haas, et al., (2001), The Journal of Histochemistry & Cytochemistry, "A comparative quantitative analysis of laminining in the basement membrane of normal, hyperplastic, and malignant oral mucosa by confocal immunofluorescence imaging", Vol. 49(10), pp. 1261-1268.
48	Hohermann, et al. (2001). Spend J. Gostroenteral, "Illegrative colitic and colorectal carginama". Vol. 7, pp. 751-758
49	Heagerty, et al., (1986), Lancet, "GB3 monoclonal antibody for diagnosis of junctional epidermolysis bullosa", Vol. 860 page 8485.
50	Heagerty, et al., (1987), British J. Dermatol, "Raid prenatal diagnosis of epidermolysis bullosa letalis using GB. monoclonal antibody", Vol. 17, pp. 271-275.
51	Henning, et al., (1999), Histopathology, "Loss of laminin-5 in the epithelium-stroma interface: an immunohistochemical marker of malignancy in epithelial lesions of the breast", Vol. 34, pp. 305-309.
52	Ulubels at al. (2001) Congar Research "Expression of the invesion feater lemining of in coloractal enginemes i
53	Hai et al. (1986) I Borred Immunology "Monoclonal artificidies to human amnion" Vol. 0, pp. 11-21
54	Kagesato, et al., (2001), Japan J. Cancer Research, "Sole expression of laminin γ 2 chain in invading tumor cells and it associateion with stromal fibrosis in lung adenocarcinomas", Vol. 21, pp. 184-192.
55	Katoh, et al., (2002), Oncology, "Correlation between laminin-5 γ 2 chain expression and epidermal growth factor receptor expression and its clinicopathological significance in squamous cell carcinoma of the tongue, Vol. 62, pp. 318-326.
56	Koshikawa, et al., (1999), Cancer Research, "Overexpression of laminin γ 2 chain monomer in invading gastric carcinom cells, Vol: 59, pp. 5596-5601.
57	Language et al. (2001) Applitical Collular Bathalagu "Laminin 5 et ahain averagaian garralates with unfavorable
58	Labil et al. (2000) APMIC "Pasament membrane laminin 5 is denocited in coloractal adaptoms and carcinomes and
59	Lucago, et al. (1900) I Cutanguage Pathal. "Tumor migroyagals in malanama avarage the heta 2 chain of lamining

EXAMINER	DATE CONSIDERED

6	60.	Määttä, et al., (2001), The Journal of Histochemistry & Cytochemistry, "Comparative analysis of the distribution of laminin chains in the basement membranes in some malignant epithelial tumors: The α l chain of laminin shows a selected expression pattern in human carcinomas", Vol. 49(6), pp. 711-725.
6	61.	Määttä, et al., (1999), Journal of Pathology, "Expression of the laminin γ2 chain in different histological types of lung carcinoma. A study by immunohistochemistry and <i>in situ</i> hybridization", Vol: 188, pp. 361-368.
6	62.	Manda, et al., (2000), Biochemical and Biophysical Research Communications, "Differential expression of the LAMB3 and LAMC2 genes between small cell and non-small cell lung carcinomas", Vol. 275, pp. 440-445.
. 6	63.	Marinkovich, et al., (1992), JBC, "The anchoring filament protein kalinin is synthesized and secreted as a high molecular weight precursor", Vol. 267, pp. 17900-17906.
6	64.	McMillan, et al., (1997), Br. J. Dermatol., "Immunohistochemical analysis of the skin in junctional epidermolysis bullosa using laminin 5 chain specific antibodies is of limited value in predicting the underlying gene mutation", Vol. 136, pp. 817-822.
6	65.	Mizushima, et al., (1998), Horm. Res., "Wide Distribution of Laminin-5 γchain in basement membranes of various human tissues", Vol. 50 (Suppl. 2), pp. 7-14.
6	66.	Mizushima, et al., (1996), J. Biochem., "Differential expression of laminin-5/ladsin subunits in human tissues and cancer cell lines and their induction by tumor promoter and growth factors", Vol. 120, pp. 1196-1202.
6	67.	Moriya, et al., (2001), Cancer, "Increased expression of laminin-5 and its prognostic significance in lung adenocarcinomas of small size", Vol: 19(6), pp. 1129-1141.
6	68.	Niki, et al., (2002), American Journal of Pathology, "Frequent co-localization of cox-2 and laminin-5 γ 2 chain at the invasive front of early-stage lung adenocarcinomas", Vol. 160(3), pp. 1129-1130.
. 6	69.	Nordemar, et al., (2001), Anticancer Research, "Laminin-5 as a predictor of invasiveness in cancer <i>in situ</i> lesions of the larynx", Vol. 21, pp. 509-512.
. 7	70.	Nordstrom, et al., (2002), Int. J. Gynecol., "Laminin-5 γ 2 chain as an invasivity marker for uni-and multifocal lesions in the lower anogenital tract", Vol. 12, pp. 105-109.
7	71.	Ono, et al., (2002), Cancer Letters, "Epidermal growth fctor receptor gene amplification is correlated with laminin-5 γ 2 chain expression in oral squamous cell carcinoma cell lines", Vol: 175, pp. 197-204.
7	72.	Patarroyo, et al., (2002), Cancer Biology, "Laminin isoforms in tumor invasion, angiogenesis and metastasis", Vol. 12, pp. 197-207.
7	73.	Patel, et al., (2002), Int. J. Cancer, "Laminin-γ2 overexpression in head-and-neck squamous cell carcinoma", Vol. 99, pp. 583-588.
7	74.	Rouselle, et al., (1991), J. Cell Biol., "Kalinin: an epithelium-specific basement membrane adhesion molecule that is a component of anchoring filaments", Vol. 114(3), pp. 567-576.
7	75.	Rouselle, et al., (1994), J. Cell Biol., "Kalinin is more efficient than laminin in promoting adhesion of primary keratinocytes and some other epithelial cells and has a different requirement of integrin receptors", Vol. 125, pp. 205-214.
7	76.	Salo, et al., (1999), Matrix Biol., "Laminin-5 promotes adhesion and migration of epithelial cells: identification of a migration-related element in the γ 2 chain gene (LAMC2) with activity in transgenic mice", Vol. 18, pp. 197-210.
7	77.	Salo, et al., (1999), Acta Univ. Oul.D 540, "Laminin-5: Function of the γ 2 chain in epithelial cell adhesion and migration, and expression in epithelial cells and carcinomas" Doctoral Dissertation.
7	78.	Seftor, et al., (2001), Cancer Research, "Cooperative interactions of laminin 5 γ 2 chain, matrix metalloproteinase-2, and membrane type-1-matrix/metalloproteinase are required for mimicry of embryonic vasculogenesis by aggressive melanoma", Vol: 61, pp. 6322-6327.
7	79.	Skyldberg, et al., (1999), Journal of the National Cancer Institute, "Laminin-5 as a marker of invasiveness in cervical lesions", Vol. 91(21), pp. 1882-1887.
8	30.	Soini, et al., (1996), Journal of Pathology, "Expression of the laminin γ 2 chain in pancreatic adenocarcinoma", Vol. 180, pp. 290-294.
8	31.	Sordat, et al., (2000), Int. J. Cancer., "Tumor cell budding and Laminin-5 expression in colorectal carcinoma can be modulated by the tissue micro-environment", Vol. 88, pp. 708-717.
8	32.	Takahashi, et al., (2002), Cancer, Cytoplasmic Expression of Laminin γ2 Chain Correlates with Postoperative Hepatic Metastasis and Poor Prognosis in Patients with Pancreatic Ductal Adenocarcinoma", Vol. 94(6), pp. 1894-1901.
8	33.	Tani, et al., (1997), American Journal of Pathology, "Pancreatic carcinomas deposit laminin-5 preferably adhere to laminin-5, and migrate on the newly deposited basement membrane", Vol: 151(5), pp. 1289-1302.

EXAMINER	DATE CONSIDERED		

84.	84. Tsuji, et al., (2002), Clinical & Experimental Metastasis, "Regulation of melanoma cell migration and invasion by laminin-5 and α3β1 integrin (VLA-3), Vol: 19, pp. 127-134.			
85.	Tunggal, et al., (2002), American Journal of Pathology, "Defective laminin 5 processing in cylindroma cells", Vol. 160(2), pp. 459-468.			
86.	Verrando, et al., (1987), Exp. Cell Res., "Monoclonal antibody GB3, a new probe for the study of human basement membranes and hemidesmosomes", Vol. 170, page 116-128.			
87.	Yamamoto, et al., (2001), Clinical Cancer Research, "Expression of the γ 2 chain of Laminin-5 at the invasive front is associated with recurrence and poor prognosis in human esophageal squamous cell carcinoma", Vol. 7, pp. 896-900.			

The Applicants hereby notify The Patent Office of the following co-pending applications:

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